APR 29 2005

6.0 510 (k) SUMMARY

SUBMITTED BY:

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NAME OF DEVICE:

Trade Name: DiaSorin LIAISON® EBNA IgG

Common Names/Descriptions: Immunoassay for the detection of IgG antibodies to EBV Nuclear Antigen (EBNA)

Classification Names: TEST, ANTIGEN, NUCLEAR, EPSTEIN-BARR VIRUS

Product Code: LLM

PREDICATE DEVICE: DiaSorin ETI-EBNA-G Kit (K946158)

DEVICE DESCRIPTION:

INTENDED USE: The DiaSorin LIAISON® EBNA IgG kit uses chemiluminescence immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative detection of specific IgG antibodies to EBV nuclear antigen synthetic peptide (EBNA) in human serum. When performed in conjunction with other EBV marker tests, this assay can be used as an aid in the clinical laboratory diagnosis of Epstein-Barr viral Syndrome in patients with signs and symptoms of EBV infection such as infectious mononucleosis (IM). LIAISON® Control EBNA IgG kit is used in conjunction with LIAISON® EBNA IgG immunoassay for quality control of assay runs.

KIT DESCRIPTION: The method for qualitative determination of specific IgG to EBNA is an indirect chemiluminescence immunoassay (CLIA). All assay steps (with the exception of magnetic particle resuspension) and incubations are performed by the LIAISON® Analyzer. The principal components of the test are magnetic particles (solid phase) coated with EBNA-1 synthetic peptide and a conjugate of mouse monoclonal antibody to human IgG linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, EBNA antibodies present in the calibrators, samples or controls bind to the solid phase. During the second incubation, the antibody conjugate reacts with EBNA IgG already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of the presence of EBNA IgG in calibrators, samples or controls.

PERFORMANCE DATA:

COMPARATIVE CLINICAL TRIALS: The clinical trials were conducted at two external US laboratories and at DiaSorin. Testing was performed on repository and prospective samples as defined below. The samples were tested by LIAISON® EBNA IgG and comparison assay, at the trial sites per the manufacturers' instructions for use.

Prospective Samples: *Subjects Sent to the Laboratory for EBV Testing:*

LIAISON® EBNA IgG	DiaSorin ETI-EBNA-G		Total
	Positive	Negative	
Positive (≥22.0 U/mL)	632	9	641
Equivocal (18.0-21.9 U/mL)	2	3	5
Negative (<18.0 U/mL)	25	152	177
Total	659	164	823

	Percent Agreement		Exact 95% confidence interval
Positive	95.9%	(632/659)	94.1 – 97.3%
Negative	92.7%	(152/164)	87.6 – 96.2%
Overall	95.3%	(784/823)	93.6 – 96.6%

Using the results for the prospective samples in three reference assays (VCA IgG, EBNA-1 IgG, VCA IgM ELISA), the samples were grouped into serological categories. Four samples tested in the LIAISON® EBNA IgG assay had insufficient volume for the entire test profile and are omitted from this analysis. The profiles and number of occurrences are presented in the following table:

	VCA IgG	VCA IgM	EBNA-1 IgG	Total
EBV seronegative	–	–	–	62
Acute infection	+	+	–	29
Past infection	+	–	+	573
Indeterminate				
VCA IgG only	+	–	–	67
VCA IgM only	–	+	–	5
EBNA IgG only	–	–	+	10
Convalescent	+	+	+	73

Based on these serological classifications, the LIAISON® EBNA IgG results for the prospective samples were compared with those obtained with the reference assay (EBNA-1 IgG ELISA).

	Percent Agreement		95% confidence interval
Acute infection	100.0%	(29/29)	90.2 – 100.0%
Past infection	98.1%	(562/573)	96.6 – 99.0%
EBV seronegative	100.0%	(62/62)	95.3 – 100.0%
Indeterminate	81.9%	(127/155)	75.0 – 87.7%
Overall	95.2%	(780/819)	93.6 – 96.6%

Retrospective Samples: *VCA IgM-positive Samples*

LIAISON® EBNA IgG	DiaSorin ETI-EBNA-G		Total
	Positive	Negative	
Positive (≥22.0 U/mL)	61	2	63
Equivocal (18.0-21.9 U/mL)	0	2	2
Negative (<18.0 U/mL)	0	5	5
Total	61	9	70

	Percent Agreement		Exact 95% confidence interval
Positive	100.0%	(61/61)	94.1 - 100.0%
Negative	N.C.*	(7/9)	N.C.*
Overall	94.3%	(66/70)	86.0 – 98.4%

*N.C. - Not Calculated – inadequate sample number

Using the results for the retrospective samples in three reference assays (VCA IgG, EBNA-1 IgG, VCA IgM ELISA), the samples were grouped into serological categories. The profiles and number of occurrences are presented in the following table:

	VCA IgG	VCA IgM	EBNA-1 IgG	Total
EBV seronegative	–	–	–	0
Acute infection	+	+	–	9
Past infection	+	–	+	0
Indeterminate				
VCA IgG only	+	–	–	0
VCA IgM only	–	+	–	0
EBNA IgG only	–	–	+	0
Convalescent	+	+	+	61

Based on these serological classifications, the LIAISON® EBNA IgG results for the retrospective samples were compared with those obtained with the reference assay (EBNA-1 IgG ELISA).

	Percent Agreement		95% confidence interval
Acute infection	55.6%	(5/9)	21.2 – 86.3%
Past infection	N/A		N/A
EBV seronegative	N/A		N/A
Indeterminate	100.0%	(61/61)	95.2 – 100.0%
Overall	94.3%	(66/70)	86.0 – 98.4%

REPRODUCIBILITY: Reproducibility studies were performed at 4 sites using a coded panel comprised of 9 frozen repository serum samples. The serum panel was prepared to represent from low- to mid-positive analyte level. The same coded panel was tested at all sites, in three replicates per run for ten runs. Results expressed in U/mL are summarized in the following table.

ID#	N	mean (U/mL)	within run S.D.	within run %CV	between run S.D.	between run %CV	between site S.D.	between site %CV	overall S.D.	overall %CV
EBS1	90	28.5	0.73	2.57	1.04	2.70	0.83	2.90	1.24	4.35
EBS2	90	62.2	4.81	6.94	8.84	11.78	3.70	5.95	15.02	24.15
EBS3	90	290.4	12.18	4.27	26.81	6.02	24.49	8.43	29.04	10.00
EB1	90	72.2	1.81	2.48	3.32	2.82	3.12	4.32	3.72	5.15
EB2	90	71.0	2.12	3.01	5.45	3.86	5.74	8.09	5.73	8.08
EB3	90	52.6	1.71	3.27	3.06	4.30	2.53	4.81	3.45	6.55
EB4	90	48.6	1.51	3.17	3.30	4.72	2.93	6.04	3.57	7.34
EB5	90	59.9	1.76	2.98	3.10	4.35	2.18	3.63	3.53	5.88
EB6	90	51.6	1.69	3.33	2.61	4.61	1.46	2.83	3.06	5.94

INTERFERENCE: Controlled studies of potentially interfering substances showed that the assay performance was not affected by hemolysis (at 1000 mg/dL hemoglobin), lipemia (at 3000 mg/dL triglycerides) and icterus (at 10 mg/dL bilirubin).

CROSS-REACTIVITY: The cross-reactivity studies for the LIAISON® EBNA IgG assay were designed to evaluate potential interference from IgG immunoglobulins directed against closely-related members of the herpes virus family (HSV-1, HSV-2, VZV, CMV, HHV6), from other organisms that may cause symptoms similar to EBV (*Toxoplasma gondii*, rubella virus) and from other conditions that may result from atypical immune system activity (rheumatoid factor (RF), anti-nuclear antibodies (ANA)). Samples for these studies were selected using commercially available devices.

Organism / condition	Number of Samples	Positive LIAISON® EBNA IgG Result
CMV IgG	19	(0/19)
VZV IgG	7	(0/7)
HSV-1 IgG	19	(1/19)
HSV-2 IgG	3	(0/3)
HHV6 IgG	1	(0/1)
Toxoplasma gondii IgG	7	(0/7)
Rubella virus IgG	30	(1/30)
ANA	1	(0/1)
RF	4	(0/4)
Total	91	(2/91)

Two specimens out of 91 total specimens tested from the disease panel were positive. There was no conclusive evidence of interference observed, however due to the limited availability of certain samples, the possibility of cross-reactivity cannot be excluded. The user is advised to perform other EBV serology assays to confirm EBV-associated infectious mononucleosis.

WARNING: Assay interference due to circulating antibodies against HIV and Hepatitis A, Hepatitis B and Hepatitis C viruses has not been evaluated. The user is responsible for establishing cross-reactivity performance with these infectious agents.

CONCLUSION

The LIAISON® EBNA IgG assay showed equivalent performance to the corresponding FDA-cleared assay. The DiaSorin LIAISON® EBNA IgG assay demonstrated agreement with the comparison method higher then 95% among prospectively collected samples and 94% agreement among retrospective selected samples. The results demonstrated that LIAISON® EBNA IgG assay can be used with the LIAISON® Analyzer for the qualitative detection of IgG antibodies to EBNA and can be intended for use as an aid in the determination of immune status to EBV.

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NAME OF DEVICE:

Trade Name: DiaSorin LIAISON® EBV IgM

Common Names/Descriptions: Immunoassay for the detection of IgM antibodies to EBV Viral Capsid Antigen (VCA)

Classification Names: EPSTEIN-BARR VIRUS, OTHER

Product Code: LSE

PREDICATE DEVICES: DiaSorin ETI-EBV-M reverse Kit (K946157)

DEVICE DESCRIPTION:

INTENDED USE: The LIAISON® EBV IgM assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative determination of specific IgM antibodies to Epstein-Barr virus (EBV) viral capsid antigen (VCA) p-18 synthetic peptide in human serum. When performed in conjunction with other EBV markers, this assay can be used as an aid in the clinical laboratory diagnosis of Epstein-Barr viral Syndrome in patients with signs and symptoms of EBV infection such as infectious mononucleosis (IM). LIAISON® Control EBV IgM kit is used in conjunction with LIAISON® EBV IgM immunoassay for quality control of assay runs.

KIT DESCRIPTION:

The method for qualitative determination of specific IgM to Epstein-Barr viral capsid antigens (VCA) is an indirect chemiluminescence immunoassay (CLIA).

All assay steps (with the exception of magnetic particle resuspension) and incubations are performed by the LIAISON® Chemiluminescence Analyzer. The principal components of the test are magnetic particles (solid phase) coated with p18 synthetic peptide and a conjugate of mouse monoclonal antibody to human IgM linked to an isoluminol derivative (isoluminol-antibody conjugate).

In the first step, samples and controls are diluted with Buffer A, which contains goat IgG to human IgG as an absorbent reagent to curb interference from human IgG specific to VCA or from rheumatoid factor. During the first incubation, VCA IgM antibodies present in the calibrators, samples or controls bind to the solid phase. During the second incubation, the antibody conjugate reacts with VCA IgM already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle.

Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of the presence of VCA IgM in calibrators, samples or controls.

PERFORMANCE DATA:

COMPARATIVE CLINICAL TRIALS: The clinical trials were conducted at two external US laboratories and at DiaSorin. Testing was performed on repository and prospective samples as defined below. The samples were tested by LIAISON® EBV IgM and comparison assay (DiaSorin ETI-EBV-M reverse ELISA Kit), at the trial sites per the manufacturers' instructions for use.

Prospective Samples: *Subjects Sent to the Laboratory for EBV Testing:*

LIAISON® EBV IgM	DiaSorin ETI-EBV-M		Total
	Positive	Negative	
Positive (≥44.0 U/mL)	58	28	86
Equivocal (36.0-43.9 U/mL)	4	10	14
Negative (<36.0 U/mL)	45	674	719
Total	107	712	819

	Percent Agreement	Exact 95% confidence interval
Positive	54.2% (58/107)	44.3 – 63.9%
Negative	94.7% (674/712)	92.8 – 96.2%
Overall	89.4% (732/819)	87.1 – 91.4%

Using the results for the prospective samples in three reference assays (VCA IgG, EBNA-1 IgG, VCA IgM ELISA), the samples were grouped into serological categories. The profiles and number of occurrences are presented in the following table:

	VCA IgG	VCA IgM	EBNA-1 IgG	Total
EBV seronegative	–	–	–	62
Acute infection	+	+	–	29
Past infection	+	–	+	573
Indeterminate				
VCA IgG only	+	–	–	67
VCA IgM only	–	+	–	5
EBNA IgG only	–	–	+	10
Convalescent	+	+	+	73

Based on these serological classifications, the LIAISON® EBV IgM results for the prospective samples were compared with those obtained with the reference assay (VCA IgM ELISA).

	Percent Agreement		95% confidence interval
Acute infection	100.0%	(29/29)	90.2 – 100.0%
Past infection	95.3%	(546/573)	93.2 – 96.9%
EBV seronegative	93.5%	(58/62)	84.3 – 98.2%
Indeterminate	63.9%	(99/155)	55.8 – 71.4%
Overall	89.4%	(732/819)	87.1 – 91.4%

Retrospective Samples: *VCA IgM-positive Samples*

LIAISON® EBV IgM	DiaSorin ETI-EBV-M		Total
	Positive	Negative	
Positive (≥44.0 U/mL)	67	0	67
Equivocal (36.0-43.9 U/mL)	0	0	0
Negative (<36.0 U/mL)	3	0	3
Total	70	0	70

	Percent Agreement	Exact 95% confidence interval
Positive	95.7% (67/70)	88.0 – 99.1%
Negative	N.C.* (0/0)	N.C.*
Overall	95.7% (67/70)	88.0 – 99.1%

*N.C.- Not Calculated – inadequate sample number

Using the results for the retrospective samples in three reference assays (VCA IgG, EBNA-1 IgG and VCA IgM ELISA), the samples were grouped into serological categories. The profiles and number of occurrences are presented in the following table:

	VCA IgG	VCA IgM	EBNA-1 IgG	Total
EBV seronegative	–	–	–	0
Acute infection	+	+	–	9
Past infection	+	–	+	0
Indeterminate				
VCA IgG only	+	–	–	0
VCA IgM only	–	+	–	0
EBNA IgG only	–	–	+	0
Convalescent	+	+	+	61

Based on these serological classifications, the LIAISON® EBV IgM results for the retrospective samples were compared with those obtained with the reference assay (VCA IgM ELISA).

	Percent Agreement	95% confidence interval
Acute infection	77.8% (7/9)	40.0 – 97.2%
Past infection	N/A	N/A
EBV seronegative	N/A	N/A
Indeterminate	98.4% (60/61)	91.2 – 100.0%
Overall	95.7% (67/70)	88.0 – 99.1%

REPRODUCIBILITY: Reproducibility studies were performed at 3 sites using a coded panel comprised of 9 frozen repository serum samples. The serum panel was prepared to represent from low- to mid-positive analyte level. The same coded panel was tested at all sites, in three replicates per run for ten runs. Results expressed in U/mL are summarized below.

ID#	N	mean (U/mL)	within run S.D.	within run %CV	between run S.D.	between run %CV	between site S.D.	between site %CV	overall S.D.	overall %CV
EMS1	90	67.2	2.22	3.30	3.36	4.26	2.21	3.28	3.92	5.83
EMS2	89	89.7	4.00	4.55	6.90	5.16	6.26	6.98	7.79	8.70
EMS3	90	<10.0	*69.6**	*7.15**	*83.6**	*6.50**	*69.5**	*7.35**	*115.7**	*12.24**
EM1	90	36.4	2.79	7.88	4.93	5.50	5.43	14.92	5.52	15.16
EM2	90	37.2	2.23	6.09	5.43	6.17	5.91	15.90	5.77	15.52
EM3	90	79.5	6.22	7.79	12.04	5.63	13.16	16.55	13.25	16.67
EM4	89	65.9	4.34	6.60	8.95	5.35	9.95	15.10	9.77	14.83
EM5	89	37.1	2.65	7.27	4.25	6.92	4.14	11.16	4.88	13.18
EM6	90	64.6	4.26	6.65	6.07	6.58	5.36	8.30	7.18	11.11

**EMS3 dose was below the reading range of the assay. Precision calculations are based on signal (RLU) for this sample.*

INTERFERENCE: Controlled studies of potentially interfering substances showed that the assay performance was not affected by hemolysis (at 1000 mg/dL hemoglobin), lipemia (at 3000 mg/dL triglycerides) and icterus (at 20 mg/dL bilirubin).

CROSS-REACTIVITY: The cross-reactivity studies for the LIAISON® EBV IgM assay were designed to evaluate potential interference from IgM immunoglobulins directed against closely-related members of the herpes virus family (HSV-1, HSV-2, VZV, CMV), from other organisms that may cause symptoms similar to EBV (*Toxoplasma gondii*, rubella virus, rubeola virus, mumps virus, hepatitis A virus, hepatitis B virus) and from other conditions that may result from atypical immune system activity (rheumatoid factor (RF), anti-nuclear antibodies (ANA)). Samples for these studies were selected using commercially available devices.

Organism / condition	Number of Samples	Positive LIAISON® EBV IgM Result
CMV IgM	29	(2/29)
VZV IgM	16	(1/16)
HSV-1 IgM	2	(0/2)
HSV-2 IgM	7	(0/7)
Hepatitis A virus IgM	10	(0/10)
Hepatitis B virus (core) IgM	23	(0/23)
Toxoplasma gondii IgM	12	(0/12)
Rubella virus IgM	11	(0/11)
Rubeola virus IgM	3	(0/3)
Mumps virus IgM	2	(1/2)
RF	6	(0/6)
ANA Ig	10	(0/10)
Total	131	(4/131)

Four specimens out of 131 total specimens tested from the disease panel were positive. There was no conclusive evidence of interference observed, however due to the limited availability of certain samples, the possibility of cross-reactivity cannot be excluded. Other EBV serology

assays should be performed to confirm EBV-associated infectious mononucleosis.

WARNING: Assay interference due to circulating antibodies against HIV and Hepatitis C virus has not been evaluated. The user is responsible for establishing cross-reactivity performance with these infectious agents.

CONCLUSION

The LIAISON® EBV IgM assay showed equivalent performance to the corresponding FDA-cleared assay. The DiaSorin LIAISON® EBV IgM assay demonstrated agreement with the comparison method higher than 89% among prospectively collected samples and 95% agreement among retrospective selected samples. The results demonstrated that LIAISON® EBV IgM assay can be used with the LIAISON® Analyzer for the qualitative detection of IgM antibodies to EBV and can be intended for use as an aid in the clinical laboratory diagnosis of Epstein-Barr viral Syndrome in patients with signs and symptoms of EBV infection such as infectious mononucleosis (IM).

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NAME OF DEVICE:

Trade Name: DiaSorin LIAISON® VCA IgG

Common Names/Descriptions: Immunoassay for the detection of IgG antibodies to EBV viral capsid antigens (VCA)

Classification Names: EPSTEIN-BARR VIRUS, OTHER

Product Code: LSE

PREDICATE DEVICE: DiaSorin ETI-VCA-G Kit (K946159)

DEVICE DESCRIPTION:

INTENDED USE: The DiaSorin LIAISON® VCA IgG kit uses chemiluminescence immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative detection of specific IgG antibodies to EBV viral capsid antigen (VCA) p-18 synthetic peptide in human serum. When performed in conjunction with other EBV marker tests, this assay can be used as an aid in the clinical laboratory diagnosis of Epstein-Barr viral Syndrome in patients with signs and symptoms of EBV infection such as infectious mononucleosis (IM). LIAISON® Control VCA IgG kit is used in conjunction with LIAISON® VCA IgG immunoassay for quality control of assay runs.

KIT DESCRIPTION: The method for qualititative determination of specific IgG to EBV viral capsid antigen (VCA) is an indirect chemiluminescence immunoassay (CLIA). All assay steps (with the exception of magnetic particle resuspension) and incubations are performed by the LIAISON® Analyzer. The principal components of the test are magnetic particles (solid phase) coated with EBV VCA p-18 synthetic peptide and a conjugate of mouse monoclonal antibody to human IgG linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, VCA IgG antibodies present in calibrators, samples or controls bind to the solid phase. During the second incubation, the antibody conjugate reacts with VCA IgG antibodies that are already bound to the solid phase. After each incubation, unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and

is indicative of the presence of EBV VCA IgG antibodies present in calibrators, samples or controls.

PERFORMANCE DATA:

COMPARATIVE CLINICAL TRIALS: The clinical trials were conducted at two external US laboratories and at DiaSorin. Testing was performed on repository and prospective samples as defined below. The samples were tested by LIAISON® VCA IgG and comparison assay (DiaSorin ETI-VCA-G ELISA Kit), at the trial sites per the manufacturers' instructions for use.

Prospective Samples: *Subjects Sent to the Laboratory for EBV Testing:*

LIAISON® VCA IgG	DiaSorin ETI-VCA-G		Total
	Positive	Negative	
Positive (≥22.0 U/mL)	717	4	721
Equivocal (18.0-21.9 U/mL)	5	0	5
Negative (<18.0 U/mL)	23	74	97
Total	745	78	823

	Percent Agreement	Exact 95% confidence interval
Positive	96.2% (717/745)	94.6 – 97.5%
Negative	94.9% (74/78)	87.4 – 98.6%
Overall	96.1% (791/823)	94.6 – 97.3%

Using the results for the prospective samples in three reference assays (VCA IgG, EBNA-1 IgG and VCA IgM ELISA), the samples were grouped into serological categories. Four samples tested in the LIAISON® VCA IgG assay had insufficient volume for the entire test profile and are omitted from this analysis. The profiles and number of occurrences are presented in the following table:

	VCA IgG	VCA IgM	EBNA-1 IgG	Total
EBV seronegative	–	–	–	62
Acute infection	+	+	–	29
Past infection	+	–	+	573
Indeterminate				
VCA IgG only	+	–	–	67
VCA IgM only	–	+	–	5
EBNA IgG only	–	–	+	10
Convalescent	+	+	+	73

Based on these serological classifications, the LIAISON® VCA IgG results for the prospective samples were compared with those obtained with the reference assay (VCA IgG ELISA).

	Percent Agreement		95% confidence interval
Acute infection	82.8%	(24/29)	64.2 – 94.2%
Past infection	98.3%	(563/573)	96.8 – 99.2%
EBV seronegative	98.4%	(61/62)	91.3 – 100.0%
Indeterminate	89.7%	(139/155)	83.8 – 94.0%
Overall	96.1%	(787/819)	94.5 – 97.3%

Retrospective Samples: *VCA IgM-positive Samples*

LIAISON® VCA IgG	DiaSorin ETI-VCA-G		Total
	Positive	Negative	
Positive (≥22.0 U/mL)	70	0	70
Equivocal (18.0-21.9 U/mL)	0	0	0
Negative (<18.0 U/mL)	0	0	0
Total	70	0	70

	Percent Agreement	Exact 95% confidence interval
Positive	100.0% (70/70)	94.1 – 100.0%
Negative	N.C.* (0/0)	N.C.*
Overall	100.0% (70/70)	94.1 – 100.0%

* N.C. - Not Calculated – Inadequate sample number

Using the results for the retrospective samples in three reference assays (VCA IgG, EBNA-1 IgG and VCA IgM ELISA), the samples were grouped into serological categories. The profiles and number of occurrences are presented in the following table:

	VCA IgG	VCA IgM	EBNA-1 IgG	Total
EBV seronegative	–	–	–	0
Acute infection	+	+	–	9
Past infection	+	–	+	0
Indeterminate				
VCA IgG only	+	–	–	0
VCA IgM only	–	+	–	0
EBNA IgG only	–	–	+	0
Convalescent	+	+	+	61

Based on these serological classifications, the LIAISON® VCA IgG results for the retrospective samples were compared with those obtained with the reference assay (VCA IgG ELISA).

	Percent Agreement	95% confidence interval
Acute infection	100.0% (9/9)	71.7 – 100.0%
Past infection	N/A	N/A
EBV seronegative	N/A	N/A
Indeterminate	100.0% (61/61)	95.2 – 100.0%
Overall	100.0% (70/70)	95.8 – 100.0%

REPRODUCIBILITY: Reproducibility studies were performed at 3 sites using a coded panel comprised of 9 frozen repository serum samples. The serum panel was prepared to represent from low- to mid-positive analyte level. The same coded panel was tested at all sites, in three replicates per run for ten runs. Results expressed in U/mL are summarized in the following table.

ID#	N	mean (U/mL)	within run S.D.	within run %CV	between run S.D.	between run %CV	between site S.D.	between site %CV	overall S.D.	overall %CV
VGS1	90	266.6	9.86	3.68	23.56	7.23	12.98	4.87	25.19	9.45
VGS2	90	52.9	1.89	3.83	3.75	5.43	2.81	5.32	4.35	8.22
VGS3	90	145.5	7.55	5.78	11.69	7.41	4.71	3.23	15.37	10.56
VG1	90	31.6	0.71	2.31	2.94	6.36	2.64	8.35	2.99	9.45
VG2	90	52.2	1.09	2.06	2.88	5.43	0.97	1.82	3.07	5.89
VG3	90	61.0	1.17	1.92	3.75	5.64	2.05	3.35	3.86	6.32
VG4	90	69.2	1.58	2.31	4.56	5.38	3.28	4.74	4.79	6.92
VG5	90	58.0	1.21	2.11	3.07	4.08	2.47	4.26	3.27	5.63
VG6	90	49.6	1.23	2.46	3.05	5.76	1.46	2.94	3.25	6.55

INTERFERENCE: Controlled studies of potentially interfering substances showed that the assay performance was not affected by hemolysis (at 1000 mg/dL hemoglobin), lipemia (at 3000 mg/dL triglycerides), icterus (at 20 mg/dL bilirubin).

CROSS-REACTIVITY: The cross-reactivity studies for the LIAISON® VCA IgG assay were designed to evaluate potential interference from IgG immunoglobulins directed against closely-related members of the herpes virus family (HSV-1, HSV-2, VZV, CMV, HHV6), from other organisms that may cause symptoms similar to EBV (Toxoplasma gondii, rubella virus) and from other conditions that may result from atypical immune system activity (rheumatoid factor (RF)).

Organism / condition	Number of Samples	Positive LIAISON® VCA IgG Result
CMV IgG	16	(1/16)
VZV IgG	7	(0/7)
HSV-1 IgG	18	(2/18)
HSV-2 IgG	3	(0/3)
HHV6 IgG	3	(0/3)
Toxoplasma gondii IgG	8	(1/8)
Rubella virus IgG	30	(0/30)
RF	4	(0/4)
Total	89	(4/89)

Four specimens out of 89 total specimens tested from the disease panel were positive. There was no conclusive evidence of interference observed, however due to the limited availability of certain samples, the possibility of cross-reactivity cannot be excluded. The user is advised to perform other EBV serology assays to confirm EBV-associated infectious mononucleosis.

WARNING: Assay interference due to circulating antibodies against HIV and Hepatitis A, Hepatitis B and Hepatitis C viruses has not been evaluated. The user is reponsible for

establishing cross-reactivity performance with these infectious agents.

CONCLUSION

The LIAISON® VCA IgG assay showed equivalent performance to the corresponding FDA-cleared assay. The DiaSorin LIAISON® VCA IgG assay demonstrated agreement with the comparison method higher then 96% among prospectively collected samples and 100% agreement among retrospective selected samples. The results demonstrated that LIAISON® VCA IgG assay can be used with the LIAISON® Analyzer for the qualitative detection of IgG antibodies to VCA p18 synthetic peptide and can be intended for use as an aid in the clinical laboratory diagnosis of Epstein-Barr viral Syndrome in patients with signs and symptoms of EBV infection such as infectious mononucleosis (IM)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

APR 29 2005

David M. Ikeda
Manager, Regulatory Affairs & Quality Systems
DiaSorin Inc.
1951 Northwestern Avenue
P.O. Box 285
Stillwater, MN 55082-0285

Re: k040120
Trade/Device Name: DiaSorin LIAISON® VCA IgG Assay
DiaSorin LIAISON® VCA IgM Assay
DiaSorin LIAISON® EBNA IgG
Regulation Number: 21 CFR 866.3235
Regulation Name: Epstein-Barr Virus Serological Reagents
Regulatory Class: Class I
Product Code: LSE, LLM
Dated: April 12, 2005
Received: April 14, 2005

Dear Mr. Ikeda:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (240)276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K040120

Device Name: LIAISON® VCA IgG

Indications For Use: The LIAISON® VCA IgG assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative determination of IgG antibodies to Epstein-Barr virus (EBV) viral capsid antigen (VCA) p-18 synthetic peptide in human serum. When performed in conjunction with other EBV markers, this assay can be used as an aid in the clinical laboratory diagnosis of Epstein-Barr viral Syndrome in patients with signs and symptoms of EBV infection such as infectious mononucleosis (IM).

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K040120

Indications for Use

510(k) Number (if known): K040120

Device Name: LIAISON® EBV IgM

Indications For Use: The LIAISON® EBV IgM assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative determination of IgM antibodies to Epstein-Barr virus (EBV) viral capsid antigen (VCA) p-18 synthetic peptide in human serum. When performed in conjunction with other EBV markers, this assay can be used as an aid in the clinical laboratory diagnosis of Epstein-Barr viral Syndrome in patients with signs and symptoms of EBV infection such as infectious mononucleosis (IM).

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

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510(k) k040120

Indications for Use

510(k) Number (if known): K040120

Device Name: LIAISON® EBNA IgG

Indications For Use: The LIAISON® EBNA IgG assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative determination of IgG antibodies to Epstein-Barr virus (EBV) nuclear antigen synthetic peptide (EBNA-1) in human serum. When performed in conjunction with other EBV markers, this assay can be used as an aid in the clinical laboratory diagnosis of Epstein-Barr viral Syndrome in patients with signs and symptoms of EBV infection such as infectious mononucleosis (IM).

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

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510(k) K040120